

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2004/008585

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl' C12N15/09, C12N1/15, C12N1/19, C12N1/21, C12N5/00, C12P21/02,
C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl' C12N15/09, C12N1/15, C12N1/19, C12N1/21, C12N5/00, C12P21/02,
C07K16/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE, BIOSIS/WPI (DIALOG)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Carter P. et al., Bispecific human IgG by design, J.Immunol.Methods, 2001, Vol.248, pages 7 to 15	3-8,10, 14-16,20
Y		1,2,9,11-13, 17-19
X	Ridgway J.B. et al., 'Knobs-into-holes' engineering of antibody CH3 domains for heavy chain heterodimerization, Protein Eng., 1996, Vol.9, pages 617 to 621	3-8,10, 14-16,20
Y		1,2,9,11-13, 17-19
X	Peipp M. et al., Bispecific antibodies targeting cancer cells, Biochem.Soc.Trans., 2002, Vol.30, pages 507 to 511	14-16,20
Y		1-13,17-19

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
19 August, 2004 (19.08.04)Date of mailing of the international search report
07 September, 2004 (07.09.04)Name and mailing address of the ISA/
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Shalaby M.R. et al., Development of humanized bispecific antibodies reactive with cytotoxic lymphocytes and tumor cells overexpressing the HER2 protooncogene, J.Exp.Med., 1992, Vol.175, pages 217 to 225	20 1-19
X A	Skerra A. et al., Use of the tetracycline promoter for the tightly regulated production of a murine antibody fragment in Escherichia coli, Gene, 1994, Vol.151, pages 131 to 135	17,19 1-16,18,20

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/JP2004/008585**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The matter common to independent claims 1, 2 and 11 to 13 (invention group A) relates to that, in producing an antibody comprising a first pair and a second pair, the contact of the first light chain not bonded to the first heavy chain with the second heavy chain not bonded to the second light chain and the contact of the first heavy chain not bonded to the first light chain with the second light chain not bonded to the second heavy chain are inhibited by, for example, expressing the first pair and the second pair at different timings. (continued to extra sheet)

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

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Continuation of Box No.III of continuation of first sheet(2)

The matter common to independent claims 3 and 4 (invention group B) relates to a process for producing an antibody comprising the step of forming a first pair, the step of forming a second pair and the step of forming the antibody with the use of the first and second pairs.

The matter common to independent claims 9 and 18 (invention group C) relates to a vector wherein the expression of the first heavy chain and the first light chain is induced by a first expression regulatory factor and a vector wherein the expression of the second heavy chain and the second light chain is induced by a second expression regulatory factor.

The matter common to independent claims 10 and 15 (invention group D) relates to an antibody composition having an antibody containing the first pair and the second pair at a high ratio.

The independent claim 17 (invention E) relates to a vector wherein the expression of a light chain or a heavy chain of an antibody is induced by an expression inducer.

Although the invention groups A to E are common to each other in relating to an antibody comprising a heavy chain and a light chain, it is obvious that this matter has been publicly known. Thus, this common matter cannot be considered as a special technical feature in the meaning of the second sentence of PCT Rule 13.2.

Moreover, there is no common matter seemingly being a special technical feature in the meaning of the second sentence of PCT Rule 13.2 in arbitrary combinations of the invention groups A to E.

Such being the case, the invention groups A to E do not comply with the requirement of unity of invention.